

In the Claims

Applicant has submitted a new complete claim set in which insertions and deletions in marked-up claims are indicated by underlining and strikeouts, respectively.

1. (Currently amended) A method of electrochemical detection of an analyte in a sample, which method comprises the steps of:

(a) providing a sensing electrode having an electroconductive polymer coating, the coating having immobilised therein or adsorbed thereto receptors which are capable of binding the desired analyte to be detected in the sample;

(b) contacting the sensing electrode with a test solution comprising the sample so that ~~said~~ the desired analyte to be detected in the sample binds to said immobilised or adsorbed receptors;

(c) contacting the sensing electrode with a solution comprising secondary receptors capable of binding to said analyte at a site spatially distinct from the site of binding to the immobilised or adsorbed receptors, said secondary receptors being conjugated with a charge label;

(d) monitoring the electric potential difference between the ~~treated~~ sensing electrode of part (c) and a reference electrode when both are immersed in an electrolyte; and

(e) monitoring the electric potential difference between the sensing electrode of part (d) and a reference electrode following a change in the ionic strength of the electrolyte at constant pH.

2. (Currently amended) A method of electrochemical detection of an analyte in a sample, which method comprises the steps of:

(a) providing a sensing electrode having an electroconductive polymer coating, the coating having immobilised therein or adsorbed thereto receptors which are capable of binding to the desired analyte to be detected in the sample;

(b) contacting the sensing electrode with a test solution comprising the sample so that said analyte binds to said immobilised or adsorbed receptors;

(c) contacting the sensing electrode with a solution comprising competing molecules capable of binding to said immobilised or adsorbed receptors, said competing molecules being conjugated with a charge label;

(d) monitoring the electric potential difference between the ~~treated~~ sensing electrode of part (c) and a reference electrode when both are immersed in an electrolyte; and

(e) monitoring the electric potential difference between the sensing electrode of part (d) and a reference electrode following a change in the ionic strength of the electrolyte at constant pH.

3. (Previously presented) A method as claimed in claim 1 wherein the charge label has the following properties:

- (i) it carries a net charge at the pH of the electrolyte of part d); and
- (ii) the magnitude of this charge changes in response to a change in the ionic strength of the electrolyte at constant pH;

4. (Previously presented) A method as claimed in claim 1 wherein the charge label has a net charge at the pH of the electrolyte of greater than one electrostatic unit.

5. (Previously presented) A method as claimed in claim 3 wherein the charge label is ferrocene, latex microspheres or gold.

6. (Currently amended) A method as claimed in claim 1 wherein steps (b) and (c) are performed simultaneously by contacting the sensing electrode with a test solution to which has been added secondary receptors ~~or competing molecules~~ conjugated with a charge label.

7. (Currently amended) A method of electrochemical detection of an analyte in a sample, which method comprises the steps of:

- (a) providing a sensing electrode having an electroconductive polymer coating, the coating having immobilized therein or adsorbed thereto receptors which are capable of binding to the desired analyte to be detected in the sample;

(b) contacting the sensing electrode with a test solution comprising the sample so that the said analyte binds to said immobilized or adsorbed receptors;

(c) contacting the sensing electrode with a solution comprising secondary receptors capable of binding to said analyte at a site spatially distinct from the site of binding to immobilized or adsorbed receptors, said secondary receptors being conjugated with an enzyme;

(d) monitoring the electric potential difference between the ~~treated~~ sensing electrode of part (c) and a reference electrode when both are immersed in an electrolyte; and

(e) monitoring the electric potential difference between the sensing electrode of part (d) and a reference electrode following exposure to an electrolyte comprising the substrate for said enzyme.

8. (Currently amended) A method of electrochemical detection of an analyte in a sample, which method comprises the steps of:

(a) providing a sensing electrode having an electroconductive polymer coating, the coating having immobilized therein or adsorbed thereto receptors which are capable of binding to the desired analyte to be detected in the sample;

(b) contacting the sensing electrode with a test solution comprising the sample so that the said the desired analyte to be detected in the sample binds to said immobilized or adsorbed receptors;

(c) contacting the sensing electrode with a solution comprising competing molecules capable of binding to said immobilized or adsorbed receptors, said competing molecules being conjugated with an enzyme;

(d) monitoring the electric potential difference between the ~~treated~~ sensing electrode of part (c) and a reference electrode when both are immersed in an electrolyte; and

(e) monitoring the electric potential difference between the sensing electrode of part (d) and a reference electrode following exposure to an electrolyte comprising the substrate for said enzyme.

9. (Previously presented) A method as claimed in claim 7 wherein the enzyme is capable of converting a substrate which has no detectable effect on the redox composition of the

electroconductive polymer coating of the sensing electrode to a product capable of directly or indirectly affecting the redox composition of the said electroconductive polymer coating.

10. (Previously presented) A method as claimed in claim 9 wherein the enzyme is a peroxidase.

11. (Previously presented) A method as claimed in claim 9 wherein the product capable of indirectly affecting the redox composition of the electroconductive polymer membrane causes a change in the pH of the electrolyte of part (e).

12. (Previously presented) A method as claimed in claim 11 wherein the enzyme is a urease.

13. (Previously presented) A method as claimed in claim 7 wherein the enzyme is capable of converting a substrate which has no detectable effect on the redox composition of the electroconductive polymer coating of the sensing electrode to a product which is a substrate for a second enzyme, the action of the second enzyme generating a second product which directly or indirectly affects the redox composition of the electroconductive polymer coating of the sensing electrode.

14. (Previously presented) A method as claimed in claim 7 wherein the enzyme is capable of converting a substrate which directly affects the redox composition of the electroconductive polymer coating of the sensing electrode to a product which has no detectable effect on the redox composition of the said electroconductive polymer coating.

15. (Currently amended) A method as claimed in claim 1 wherein the ~~receptor molecules~~ receptors or secondary receptors are monoclonal antibodies, polyclonal antibodies, antibody fragments, antibody mimics, chimaeric antibodies viral lysates, recombinant proteins, synthetic peptides, hormones, hormone receptors, single stranded nucleic acids, low molecular weight molecules, chemical compounds conjugated with proteins (~~haptens~~), haptens, fragments of bacterial, plant or animal cells, lectins, glycoproteins or carbohydrates.

16. (Previously presented) A method as claimed in claim 1 wherein the electroconductive polymer coating of the sensing electrode has been doped with dopant anions.
17. (Previously presented) A method as claimed in claim 16 wherein the dopant anions are dodecyl sulphate or dextran sulphate.
18. (Currently amended) A method as claimed in claim 1 wherein steps (b) and (c) are performed simultaneously by contacting the sensing electrode with a test solution to which has been added secondary receptors ~~or competing molecules~~ conjugated with an enzyme label.
19. (Previously presented) A method as claimed in claim 1 wherein the sensing electrode comprises adaptor molecules immobilized in or adsorbed to the electroconductive polymer coating thereof and the receptors capable of binding to the analyte to be detected are attached to the said adaptor molecules.
20. (Currently amended) A method as claimed in claim 19 wherein steps (b) and (c) are performed simultaneously with a step of contacting the sensing electrode with receptors by contacting the sensing electrode having adaptor molecules immobilised in or adsorbed to the electroconductive polymer layer with a test solution to which has been added receptors and secondary receptors ~~or competing molecules~~ conjugated with a charge label or enzyme.
21. (Currently amended) A method as claimed in claim 19 wherein the adaptor molecules are molecules capable of binding to at least one class of ~~receptor molecules~~ receptors capable of binding to the said analyte.
22. (Previously presented) A method as claimed in claim 19 wherein the receptors capable of binding to the analyte to be detected are biotinylated, the adaptor molecules are avidin or streptavidin and the receptors are attached thereto via a biotin/avidin or biotin/streptavidin binding interaction.

23. (Previously presented) A method as claimed in claim 19 wherein the receptors capable of binding to the analyte to be detected are antibodies, the adaptor molecules are protein A or protein G and said antibodies are attached thereto via a protein A/antibody or protein G/antibody binding interaction.

24. (Previously presented) A method as claimed in claim 19 wherein the receptors capable of binding to the analyte to be detected contain a sugar moiety, the adaptor molecules are lectins and the receptors are attached thereto via a lectin/sugar binding interaction.

25. (Previously presented) A method as claimed in claim 19 wherein the receptors capable of binding to the analyte to be detected are labelled with FITC, the adaptor molecules are anti-FITC antibodies and the receptors are attached thereto via an FITC/anti-FITC binding interaction.

26. (Previously presented) A method as claimed in claim 1 in which biological fluids such as whole blood, serum, lymph, urine, saliva, cerebrospinal fluid or semen are used as the test solution.

27. (Previously presented) A method as claimed in claim 1 wherein at least steps (d) and (e) are carried out in a flow-through measuring cell.

28. (Currently amended) A method as claimed in claim 19 wherein the step of providing a sensing electrode having adaptor molecules immobilized in the electroconductive polymer coating comprises producing the ~~said~~ sensing electrode using a method comprising steps of:

- (a) preparing an electrochemical polymerisation solution comprising monomeric units of the electroconductive polymer and adaptor molecules,
- (b) immersing an electrically conductive electrode in the electrochemical polymerisation solution, and
- (c) applying a cyclic electric potential between the ~~said~~ sensing electrode and the electrochemical polymerisation solution to coat the electrode by electrochemical synthesis of the polymer from the solution, said cyclic electric potential being applied for at least one full cycle.

29. (Currently amended) A method as claimed in claim 19 wherein the step of providing a sensing electrode having adaptor molecules adsorbed to the electroconductive polymer coating comprises producing the ~~said~~ sensing electrode using a method comprising steps of:

- (a) preparing an electrochemical polymerisation solution comprising monomeric units of the electroconductive polymer,
- (b) immersing an electrically conductive electrode in the electrochemical polymerisation solution,
- (c) applying a cyclic electric potential between the electrode and the electrochemical polymerisation solution to coat the electrode by electrochemical synthesis of the polymer from the solution, said cyclic electric potential being applied for at least one full cycle; and
- (d) contacting the coated electrode with a solution comprising adaptor molecules such that the adaptor molecules are adsorbed onto the electroconductive polymer coating of the electrode.

30. (Previously presented) A method as claimed in claim 28 wherein the adaptor molecules are selected from the group consisting of avidin, streptavidin, anti-FITC antibodies and a molecule capable of specifically binding to at least one class of receptor molecules.

31. (Previously presented) A method as claimed in claim 28 wherein monomeric units of the electroconductive polymer are pyrrole, thiophene, furan or aniline.

32. (Previously presented) A method as claimed in claim 28 in which a dopant salt is added to the electrochemical polymerisation solution.

33. (Previously presented) A method as claimed in claim 32 wherein the salt is sodium dodecylsulphate or sodium dextran sulphate.

34. (Previously presented) A method as claimed in claim 28 wherein the cyclic electric potential has a sawtooth form.

35. (Previously presented) A method as claimed in claim 28 wherein the cyclic electric potential is applied for at least two cycles.

36. (Previously presented) A method as claimed in claim 28 wherein the cyclic electric potential has a peak value applied to the electrode which is less than or equal to +2 volts.

37. (Currently amended) A method of electrochemical detection of an analyte in a sample, which method comprises the steps of:

(a) providing a sensing electrode comprising an electrically conductive electrode coated with a layer of electroconductive polymer with molecules of avidin or streptavidin immobilized therein or adsorbed thereto, said avidin or streptavidin molecules being attached to receptor ~~molecule~~ molecules capable of binding the analyte to be detected attached via a biotin/avidin or biotin/streptavidin binding interaction;

(b) contacting the sensing electrode with a test solution comprising the sample so that said desired analyte binds to said immobilized or adsorbed receptor molecules;

(c) monitoring the potential of the sensing electrode relative to a reference electrode when both are immersed in an electrolyte; and

(d) monitoring the potential difference of the sensing electrode relative to the reference electrode following a change in the ionic strength or composition of the electrolyte at constant pH.

38. (Previously presented) A method as claimed in claim 37 wherein the analyte to be detected is a nucleic acid and the receptor molecules are oligonucleotides.

39-42 (Canceled)

43. (New) A method as claimed in claim 2 wherein steps (b) and (c) are performed simultaneously by contacting the sensing electrode with a test solution to which has been added competing molecules conjugated with a charge label.

44. (New) A method as claimed in claim 2 wherein steps (b) and (c) are performed simultaneously by contacting the sensing electrode with a test solution to which has been added competing molecules conjugated with an enzyme label.
45. (New) A method as claimed in claim 2 wherein the sensing electrode comprises adaptor molecules immobilized in or adsorbed to the electroconductive polymer coating thereof and the receptors capable of binding to the analyte to be detected are attached to the said adaptor molecules.
46. (New) A method as claimed in claim 45 wherein steps (b) and (c) are performed simultaneously with a step of contacting the sensing electrode with receptors by contacting the sensing electrode having adaptor molecules immobilised in or adsorbed to the electroconductive polymer layer with a test solution to which has been added receptors and competing molecules conjugated with a charge label or enzyme.